UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,464	05/03/2007	Marsha A. Moses	C1285.70006US01	5882

23628 7590 11/09/2011
WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
DENT, ALANA HARRIS	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
11/09/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,464	MOSES ET AL.	
	Examiner	Art Unit	
	Alana Harris Dent, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☐ Claim(s) *1,3,4,6,7,9-16 and 20-37* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1, 3, 4, 6, 7, 9-16 and 20-37* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/05/09; 05/25/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 1, 3, 4, 6, 7, 9-16 and 20-37 are pending.

Claims 1 and 10 have been amended.

Claims 1, 3, 4, 6, 7, 9-16 and 20-37 are examined on the merits.

Withdrawn Grounds of Objections

Claim Objections

2. Claims 1, 4, 7 and 10 are no longer objected to because Applicants have presented persuasive arguments noting the claims are not limited to the detection of ADAM 12 protein, see Remarks filed September 15, 2011, page 7.

Withdrawn Grounds of Rejection

Claim Rejections - 35 USC § 112

3. The rejection of claims 1, 3, 10-16 and 20-25 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicants' amendments to claims 1 and 10.

Maintained Rejections

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The rejection of claims 1, 3, 4, 6, 7, 9-16 and 20-37 under 35 U.S.C. 103(a) as being unpatentable over Iba et al. (Am J. Pathol. 154(5):1489-501, May 1999), and further in view of Berger et al./ U.S. Patent Application Publication number 2003/0148410 A1 (filed November 21, 2002) is maintained.

Applicants cite several passages in the MPEP in support of their arguments, see pages 8 and 9. Applicants continue to argue the secreted form of ADAM (ADAM 12-S) does not differentiate between cancer and normal tissues as noted in Iba, see Remarks, page 8, 3rd paragraph; and Iba, page 1493, 2nd column. Applicants reiterate "one of ordinary skill in the art...would not have a reason to use any form of ADAM 12 to diagnose cancers of epithelial origin in the biological fluids as instantly claimed", see page 8 of the Remarks, 3rd paragraph. These arguments and points of view have been carefully considered, but found unpersuasive.

Applicants' arguments seem to be based upon limitations that are not of record in the claims. The claims do not differentiate between the particular forms of ADAM 12 that is detected. The claims do not include a detection step with any particular antibody, which could possibly discriminate between membrane-anchored long form (ADAM 12-L) and the shorter secreted form (ADAM 12-S). Nevertheless, it would be reasonable to one of ordinary skill in the art to test a plethora of biological samples, including urine for ADAM 12. Both, Iba and Berger provide impetus to do such, see Iba, Figure 1 on page 1494; and Berger, page 4, section 0058.

The Examiner is fully aware of the tenets of formulating a formidable 103 rejection and reiterates that she has set forth rejection. It is clear while Iba is silent in regard to assaying a biological sample that is a fluid, particularly urine, Berger sets forth the motivation and reasoning to apply the teachings of Berger to Iba. Iba presents the role of ADAM proteins in cell adhesion should be further studied and their instant paper may initiate such, see page 1500, 1st column, last sentence before "Acknowledgements". Berger provides a reasonable expectation of success to assay the presence of a marker protein in a biological sample including fluids given these assays are routinely conducted and diagnostic, see page 31, beginning at section 0276.

It would have still been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention to further gain knowledge on ADAM

expression and its correlation with cancer. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Iba and Berger to obtain a plethora of biological samples to sample for ADAM, a potential biomarker. The rejection is maintained and made for the reasons of record and set forth herein.

Iba teaches "[t]he distribution of ADAM 12 in... 37 human carcinomas compared with the normal counterpart tissue... investigated by immunohistochemistry", see page 1493, Results section. These tissue specimens are from human carcinomas comprising ductal breast carcinoma, adenocarcinoma of the colon and rectum, squamous cell carcinoma of the lung and adenocarcinoma of the stomach, see page 1490, Tissue samples...section. Adjacent nontumorous tissues were also investigated. "All 15 cases of breast carcinomas exhibited intense ADAM 12 immunoreactivity (Figure 1A) using several different antibodies, whereas in normal breast tissue, only a few scattered luminal cells of the ducts exhibited ADAM 12 immunoreactivity (Figure 1E)", see page 1493, Results section. Labeled monoclonal antibodies to human ADAM 12 were implemented in the immunohistochemistry assays, see page 1490, Antibodies and Immunohistochemistry...sections; and Figure 1 on page 1494.

Normal and cancerous human breast tissue specimens were analyze by RT-PCR using specific primers for ADAM 12-L and ADAM 12-S, see last sentence

of column 1, page 1493; and Figure 1 on page 1494. "Breast carcinoma tissue appeared to contain more ADAM 12-L transcript than normal breast tissue (Figure 1G)", see bridging sentence of columns 1 and 2 on page 1493. Iba does not teach fluid biological samples. Iba does not teach the disclosed method, wherein a urine sample is assayed for ADAM 12.

However, Berger teaches urine as a biological sample to test for the presence of ADAM 12. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of both documents assay a plethora of biological samples for ADAM 12, particularly a urine sample. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings because the Berger implemented the diagnostic assay using urine as a test sample and ADAM 12 is clearly and definitively associated with tumor cancer, see publication, page 1, section 0008 and page 33, section 0300; and Iba, abstract.

6. The rejection of claims 1, 3, 4, 6, 7, 9-16 and 20-37 under 35 U.S.C. 103(a) as being unpatentable over Iba et al. (Am J. Pathol. 154(5):1489-501, May 1999), and further in view of WO document, WO 01/66557 A1 (published 13 September 2001/ IDS reference number 3 submitted May 25, 2010) and Berger et al./ U.S.

Patent Application Publication number 2003/0148410 A1 (filed November 21, 2002).

Applicants' arguments are similar to those presented in the initial 103(a) rejection. These arguments and points of view have been carefully considered, but found unpersuasive.

Applicants' arguments seem to be based upon limitations that are not of record in the claims. The claims do not differentiate between the particular forms of ADAM 12 that is detected. The claims do not include a detection step with any particular antibody, which could possibly discriminate between membrane-anchored long form (ADAM 12-L) and the shorter secreted form (ADAM 12-S). Nevertheless, it would be reasonable to one of ordinary skill in the art to test a plethora of biological samples, including urine for ADAM 12.

Applicants are reminded the claims broadly read on a number of fluid biological samples, as well as the broadly termed ADAM 12. The claims do not include a detection step with any particular antibody, which could possibly discriminate between membrane-anchored long form (ADAM 12-L) and the shorter secreted form (ADAM 12-S), nor read on just urine. Notwithstanding, it is art known that cancer cells abrogate organs, vasculature and would be present in fluids, such as sera and blood. Consequently, both forms of ADAM 12 would have a high propensity to be detected and it would be expected by one of ordinary skill in the art to detect the membrane-bound form of ADAM in

biological fluids. While Berger does discuss detecting colon cancer, the patent is not devoid of teaching identifying breast cancer with the assaying a urine sample, see page 4, column 0058. For these reasons and the reasons of record the rejection is maintained and reiterated.

Iba teaches "[t]he distribution of ADAM 12 in... 37 human carcinomas compared with the normal counterpart tissue... investigated by immunohistochemistry", see page 1493, Results section. These tissue specimens are from human carcinomas comprising ductal breast carcinoma, adenocarcinoma of the colon and rectum, squamous cell carcinoma of the lung and adenocarcinoma of the stomach, see page 1490, Tissue samples...section. Adjacent nontumorous tissues were also investigated. "All 15 cases of breast carcinomas exhibited intense ADAM 12 immunoreactivity (Figure 1A) using several different antibodies, whereas in normal breast tissue, only a few scattered luminal cells of the ducts exhibited ADAM 12 immunoreactivity (Figure 1E)", see page 1493, Results section. Labeled monoclonal antibodies to human ADAM 12 were implemented in the immunohistochemistry assays, see page 1490, Antibodies and Immunohistochemistry...sections; and Figure 1 on page 1494. Iba does not teach the disclosed method, wherein a biological sample assayed for ADAM 12 is urine.

The WO document teaches a protein encoded by gene no: 2 is human ADAM12 protein, see page 12, section 41. Antibodies directed to this protein

are used for the diagnosis of diseases in a biological sample, see page 13, section 44; page 14, section 46; page 59, section 178; page 89, section 266; and page 90, sections 267-269. Biological samples include body fluids (such as sera, plasma, urine) and tissue biopsies, see page 97, section 297; page 107, section 329; and pages 108-109. The antibodies can be used in methods of diagnosis of cancers such as gastric, ovarian, lung, liver, breast and bladder, see section 427 bridging section 427. Moreover, Berger discloses not only can colon cancer be diagnosed or identified, but ovarian, lung, cervical, breast and prostate cancer may also be identified using the taught methodology, see page 3, section 0048; page 4, section 0058; and page 11, section 0118. The ADAM 12 marker can be detected blood fluids, stool, colon lavage fluids, lymph fluids and urine via an antibody which is labeled by several means, see page 3, section 0048; page 10, section 0114; and page 33, section 0300.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine all the teachings of all the documents to assay a plethora of biological samples for ADAM 12, particularly a urine sample, blood or serum. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Berger. Berger implemented a diagnostic assay using urine, blood fluids as test samples and ADAM 12 is clearly and definitively associated with cancer, see

WO document; Berger, page 3, section 0048 and page 33, section 0300; and

Iba, abstract.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. The provisional rejection of claims 1, 3, 4, 6, 7, 9-16 and 20-37 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21, 23 and 42 of copending Application No.

12/085,134/ U.S. Patent Application No. 20090215102 (filed April 14, 2009) is maintained.

Applicants simply assert once again when the pending claims are found allowable, Applicants will address the rejection, see Remarks submitted September 15, 2011, page 12. This point of view has been carefully considered, but found unpersuasive. The rejection is maintained for the reasons of record. The rejection is reiterated.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims read detecting ADAM 12 in biological samples.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory

action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a ***flexible schedule***, however she can normally be reached between the hours of 8 am to 8 pm, Monday through Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Misook Yu, Ph.D. can be reached on (571) 272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.
7 November 2011

/Alana M Harris, Ph.D./

Primary Examiner, Art Unit 1643